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QUANTITATIVE RELATIONS BETWEEN AMBOCEPTOR AND THE SERUM OF COMPLEMENT-DEFICIENT GUINEA-PIGS

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Through the courtesy of Dr. F. A. Rich, head of the veterinary department of the Vermont Agricultural Experiment Station, I received a number of guinea-pigs from a breed naturally deficient in complement. According to Moore,[1] this characteristic property is inheritable. Both Moore and Downing (cited by Moore [1]) found that in some instances as much as 1 c c of the serum produced no hemolysis of sensitized corpuscles. Moore also found that the apparent lack of complement in the blood serum of some guinea-pigs is not due to the presence therein of anything interfering with the action of the amboceptor. Coca [2] recently reported that both the mid-piece and the end-piece of the complements of these guinea-pigs are present. "There is lacking only the so-called 'third piece,' addition of inactive guinea-pig or human serum containing this third component to the deficient serum causes hemolysis in about three times the minimal hemolytic quantity of normal guinea-pig's serum." The third component according to this author is not identical with the lipoid cytozyme (thrombokinase), since the blood of the complement-deficient guinea-pigs clots normally.

Having found 2 guinea-pigs, the serums of which failed to hemolyze 0.5 c c of a 5 % suspension of sensitized sheep corpuscles in doses of 0.8 and 1.0 c c, it was thought of interest to find out whether an increase of amboceptor alone will produce activation of the deficient serum. The amboceptor was employed in doses of 2, 10, 50, 100 and 500 units. The unit of cells was 0.5 c c of a 5% suspension of sheep corpuscles. The complement-deficient serums were employed in doses of 0.1 c c. The incubation period was 1 hour at 37 C. Table 1 shows clearly the effect of the increased amboceptor content. Complete hemolysis occurred in the tube containing 500 units of amboceptor. The complement was employed in doses of 0.1 c c, thus 8 and 10 times

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[1] J. Immunol., 1919, 4, p. 425.

[2] Proc. Soc. Exper. Biol. & Med., 1920, 18, p. 71.

less than an amount which in itself failed to hemolyze 0.5 c c of a 5% suspension of corpuscles sensitized with 2 units of amboceptor. The serums of both guinea-pigs reacted equally, while in none of the control tubes was hemolysis observed.

In a subsequent experiment an attempt was made to activate and accelerate the reaction of the deficient serum by the addition of inactive normal guinea-pig, human, dog, horse, sheep and rabbit serums. As a control egg albumin was used. Jonas[3] was able to activate by means of inactivated serums complement which had been inactivated by cobra venom; the power of these various serums varied in their capacity for activation. He found horse serum to be a weak activator, while swine serum proved to be extraordinarily strong, acting in dilutions from 1:20,000 to 1:40,000 of 1 c c. Of 15 human serums only 4 activated the cobra venom inactive complement. In our experiment with complement-deficient guinea-pig serums and the sheep hemolytic system, both human and guinea-pig serums acted powerfully. The human serum employed, however, was pooled. Horse serum was a weak accelerator and sheep and rabbit serums still weaker or they did

TABLE 1

THE EFFECT OF INCREASED AMBOCEPTOR UNITS ON THE ACTIVATION OF THE SERUM OF COMPLEMENT-DEFICIENT GUINEA-PIGS

Guinea-Pigs	Amount of Serum in C c	Units of Amboceptor per 0.5 C c	Cell Suspension, 5 % in C c	Result	Remarks
1	1.0	2	0.5	No lysis	
2	0.8	2	0.5	No lysis	
		500	0.5	No lysis	Agglutination
		Salt sol.	0.5	No lysis	
		Salt sol.	0.5	No lysis	To this tube 0.1 c c. glycerol was added*
1	0.1	...	0.5	No lysis	
2	0.1	...	0.5	No lysis	
1	0.1	2	0.5	No lysis	
	0.1	10	0.5	Trace of lysis	
	0.1	50	0.5	Slight lysis	Agglutination
	0.1	100	0.5	Marked lysis	Agglutination
	0.1	500	0.5	Complete lysis	Agglutination
2	0.1	2	0.5	No lysis	
	0.1	10	0.5	Trace of lysis	
	0.1	50	0.5	Marked lysis	Agglutination
	0.1	100	0.5	Almost complete lysis	Agglutination
	0.1	500	0.5	Complete lysis	Agglutination

* Amboceptor was glycerolated 50%.

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[3] Ztschr. f. Immunitätsf., 1913, 17, p. 539.

not act at all. Dog serum acted less vigorously than guinea-pig serum. Egg albumin failed entirely, indicating that serum alone contributes some substance or condition which accelerates the reaction. As controls the various inactive serums were added to cells with increasing doses of amboceptor. It was found that the heated guinea-pig serum (0.1 c c) added to 500 units of amboceptor and 0.5 c c of 5% corpuscles led to complete hemolysis of the agglutinated cells. Dog serum gave marked hemolysis while the other serums remained inactive. In the presence of inactive human serum, complete lysis took place with 0.1 c c of guinea-pig serum, while 0.005 c c of this serum acted only in the presence of 500 units of amboceptor. The smallest quantity of activator (human serum) necessary for complete lysis was 0.0001 c c in the presence of 500 units of amboceptor; 0.001 c c of human serum increased distinctly the effect of deficient guinea-pig serum.

DISCUSSION

These observations indicate that a greatly increased amboceptor content is capable of rendering the sheep cells so sensitive that the complement-deficient serum induces lysis in doses which in themselves are entirely inactive in the presence of the usual amboceptor amounts. Whether the amboceptor itself supplements the so-called third component of Ritz[4] is difficult to state. The addition of normal inactive rabbit serum to this system as an activator practically failed, while the addition of normal inactive human or guinea-pig serums greatly enhanced the reaction.

Of particular interest is the fact that in the presence of such large amounts of amboceptor following agglutination some normal inactive guinea-pig serum may produce lysis. There seems to be a similarity in the behavior of the deficient serums to cobra venoms inactive serums or serums whose complement has been inactivated by yeast cells and bacteria as indicated by Coca. When mixed with small quantities of normal inactive serums the complement-deficient serum produces lysis in smaller doses and also with increased velocity. The question whether this is due to an unknown third component or a certain physical state is still problematic. The results indicate clearly that different inactive serums have a variable degree of activating power, thus in large part confirming the work of Jonas.

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[4] Ztschr. f. Immunitätsf., 1912, 13, p. 62.

SUMMARY

The serums of complement deficient guinea-pigs have been studied and their great deficiency as noted by Downing and Moore confirmed.

The deficient action is not due to amboceptor interference because the increase of amboceptor leads to hemolysis of the cells. These serums when employed in comparatively small doses (0.1 c c) and in the presence of 500 units of hemolysin readily cause lysis.

The deficient serums react in a similar manner as cobra vemon inactive serums in that the addition of normal inactive homologous or heterologous serums will markedly enhance hemolysis, confirming the results of Coca.

Various inactive serums have varying degrees of activating power when added to the deficient serum amboceptor cell mixture. The same phenomenon was observed by Jonas in the case of cobra venom inactivated serum.

By the increase of amboceptor and the addition of normal inactive homologous or heterologous serums the deficient serum has been made to act within the usual lytic range of normal guinea-pig serum.